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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,263	01/11/2006	Kersten M. Small	24026-10318	5287

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EXAMINER	
HOWARD, ZACHARY C	
ART UNIT	PAPER NUMBER
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,263	SMALL ET AL.	
	Examiner	Art Unit	
	ZACHARY C. HOWARD	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6,11-13 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6,11-13 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission filed on 12/11/08 has been entered.

Status of Application, Amendments and/or Claims

The amendment of 12/11/08 has been entered in full. Claims 1, 3 and 13 are amended. Claims 4, 5, 7-10, 14-17 and 19-23 were previously canceled.

Claims 1-3, 6, 11, 12, 13 and 18 are pending and under consideration.

Withdrawn Objections and/or Rejections

The following page numbers refer to the previous Office Action (9/11/08).

The objection to claim 13 at pg 3 for failing to further limit claim 6 is *withdrawn* in view of Applicants' amendments to the claims.

The rejection of claims 1-3, 6, 11-13 and 18 at pg 4-5 under 35 U.S.C. 101 for being directed to non-statutory subject matter is *withdrawn* in view of Applicants' amendments to claims 1 and 2.

The objection to the specification at pg 5-6 for introducing new matter into the disclosure is *withdrawn* in view of Applicants' amendments to page 1 of the specification.

The rejection of claims 1-3, 6, 11-13 and 18 under 35 U.S.C. § 112, first paragraph at pg 6-7 as containing new matter is *withdrawn* in view of Applicants' amendments to the claims.

Specification

The disclosure is objected to because of the following informalities:

The title of the invention "METHODS OF CARDIOVASCULAR DISEASE ASSESSMENT IN AN INDIVIDUAL" is not descriptive because it encompasses methods of assessment much broader in scope than the recited claim. A new title is required that is clearly indicative of the invention to which the claims are directed. The title should reflect the specific cardiovascular disease recited in the claim ("heart failure") and the basis for such assessment (i.e., polymorphisms in specific adrenergic receptors).

Appropriate correction is required.

New Rejections

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3, 6, 11-13 and 18 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 7,449,292 (published 11/11/08, filed 9/13/04 and claiming priority to 9/12/03). The instant application and the '292 patent share inventor Stephen Liggett. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

The recitation of “of predicting relative efficacy of a beta blocker therapy in a subject” in the preamble of claim 1 of the '292 patent is interpreted as an intended use and bears no accorded patentable weight to distinguish the claimed method of the patent from the instant claimed method. In particular, it is noted that the method of claim 1 ('292) does not actually require administration of a beta blocker (e.g. carvedilol), only a prediction of efficacy were it to be administered.

The first method step of claim 1 ('292) is directed to "determining from a sample from the subject the presence or absence of a polymorphism in a β_1-adrenergic receptor in the sample from the subject, wherein the polymorphism comprises arginine at position 389". This method step is the same in scope as method step (b) of claim 1 of the instant application, which recites "detecting the presence or absence of an arginine at position 389 of a beta-1 adrenergic receptor (β_1Arg389) in a sample from an individual".

The method steps of claim 1 ('292) do not specify detection of a polymorphism in the α2c adrenergic receptor, as is recited in method step (a) of instant claim 1. However, the method of claim 1 ('292) uses "comprising" language, indicating that other, unrecited steps are encompassed by the method. Furthermore, the portion of the disclosure informing claim 1 of the '292 patent teaches that "[i]n additional embodiments, the identity of at least one polymorphism in an α2c is determined, alone or in combination with one or more polymorphisms of either or both of the β_1-AR and the β_1-AR" (pg 13, lines 40-44)". Furthermore, the only specific polymorphism of the α2c adrenergic receptor that is taught in the specification is "del322-325", which is taught as "especially preferred" (pg). Thus, the portion of the disclosure informing claim 1 ('292) teaches as a preferred embodiment a method comprising a further step of detecting a

polymorphism of the α2c adrenergic receptor that is a deletion of amino acids 322-325, as is recited in step (a) of instant claim 1.

Claim 1 ('292) ends with a step of "predicting relative efficacy of a beta blocker therapy" and follows with a wherein clause that states "wherein the beta blocker therapy comprises administering carvedilol, based on the presence or absence of the polymorphism, the presence of the polymorphism indicating a relatively greater efficacy of the beta blocker therapy in the subject, wherein the subject is heterozygous or homozygous for the polymorphism, as compared to a subject lacking the polymorphism". Together, the final step of claim 1 ('292) and the wherein clause inherently result in an assessment that meets step (c) of instant claim 1, for the following reasons.

The "predicting" step and "wherein" clause of claim 1 ('292) include predicting greater efficacy of beta blocker therapy based on the presence of a homozygous Arg-389 in the β_1-adrenergic receptor. The teachings of specification of the '292 patent intrinsically link the efficacy of beta blocker therapy with the risk of heart failure. In Example 3, the '292 patent teaches that when heart failure patients were treated with carvedilol "Arg389-homozygous patients showed greater improvement in LVEF … compared with Gly389-homozygous patients". Based on these results, the specification teaches in the next paragraph that, "Thus, the Arg 389 variant predisposes a carrier to heart failure". Thus, the '292 patent teaches that predicting the efficacy of a beta blocker by determining the phenotype of the β_1-adrenergic receptor also inherently determines the risk of heart failure in said patient. Such teachings inherently inform claim 1 of the '292 patent. Thus, practicing claim 1 and predicting that a subject with a homozgygous Arg 389 variant would experience a greater response to carvedilol would inherently also assess that said individual is "at increased risk of heart failure". This assessment would remain the same even if a homozygous α_{2c}DEL322-325 is also found in said patient. Thus, the "predicting" step of claim 1 ('292) inherently meets the limits of step (c) of instant claim 1.

In summary, a preferred embodiment of claim 1 of the '292 patent (as informed by the teachings of the specification regarding preferred the embodiments of the claimed invention) anticipates the limitations of instant claim 1.

Instant claim 2 depends from claim 1 and encompasses a sample that is a tissue sample. The portion of disclosure informing claim 1 ('292) teaches that the polymorphisms can be detected in affected tissues (see Example 3 of the '292 patent). Therefore, claim 1 of the '292 patent also anticipates instant claim 2.

Instant claim 3 depends from claim 1 and limits at least one of the detecting steps to being performed using a nucleic acid or protein assay. The portion of disclosure informing claim 1 ('292) teaches that the polymorphisms can be detected using nucleic acid assays (col 9, lines 36-39 of the '292 patent). Therefore, claim 1 of the '292 patent also anticipates instant claim 3.

Instant claims 6 and 11 depend from claim 1 and each encompass that the method further comprises "the step of selecting a therapy regimen based on the presence of both the α_{2c}DEL322-325 polymorphism and the β_1Arg389 polymorphism, wherein the therapy regimen delays development of heart failure in the individual", and further wherein the regimen comprises administration of an antagonist of β_1Arg389. Claim 1 ('292) meets this limitation as well, because predicting that the beta blocker (which is "an antagonist of β_1- Arg389" and a form of therapy that delays development of heart failure) has greater efficacy in a patient with a homozygous β_1-Arg389 meets the limitation that the beta blocker is "selected". According to the teachings of the '292 patent, this "selection" would remain the same even if a homozygous α_{2c}DEL322-325 was also found in said patient. As noted above, the '292 patent specifically teaches additional determination of polymorphisms in the α_{2c} adrenergic receptor as a preferred embodiment, and includes the α_{2c}DEL322-325 polymorphism as a preferred embodiment. Therefore, claim 1 of the '292 patent also anticipates instant claims 6 and 11.

Instant claim 12 depends from claim 6 and limits the therapy regimen to lifestyle changes. This is met by the same limitation as claim 6, because administration of a beta blocker is a life style change; therefore selecting a beta blocker is a form of selecting a

therapy that is a life style change. Therefore, claim 1 of the '292 patent also anticipates instant claim 6.

Claim 13 depends from claim 1 and recites a limitation similar to claim 6, except that the wherein clause states that "the therapy regimen delays early death associated with heart failure". Claim 1 ('292) meets the limitations of this claim for the same reasons as claim 6 because a beta blocker is inherently a therapy regimen that delays early death associated with heart failure. Therefore, claim 1 of the '292 patent also anticipates instant claim 13.

Claim 18 depends from claim 1 and recites the further step of "counseling the individual regarding the potential risk of developing a heart failure based on the presence of both the β_1- Arg389 polymorphism and the α_{2c}DEL322-325 polymorphism". This additional step is inherently met by the disclosure of the '292 patent that informs the claimed method, because said disclosure includes the statement that the "Arg 389 variant predisposes a carrier to heart failure" in the teachings that inform the method of claim 1 ('292). The term "counseling the individual" includes publishing such potential risk in a public document such as a published patent. Therefore, claim 1 of the '292 patent also anticipates instant claim 18.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Z. C. H./
Examiner, Art Unit 1646

/Bridget E Bunner/
Primary Examiner, Art Unit 1647